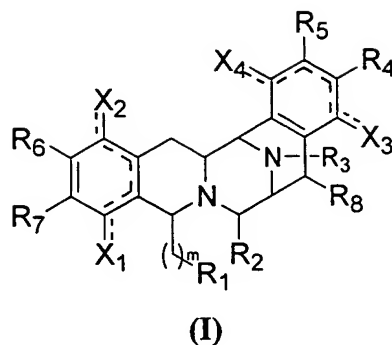


CLAIMS

1. A compound having the structure (I):



wherein R₁ is NR_AR_B, -OR_A, -SR_A, -C(=O)R_A, -C(=S)R_A, -S(O)₂R_A, or an aliphatic, heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently hydrogen, -(C=O)R_C, -NHR_C, -(SO₂)R_C, -OR_C, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or R_A and R_B, when taken together form an aryl, heteroaryl, cycloaliphatic, or cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, -OR_D, -SR_D, -NHR_D, -(C=O)R_D, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R₂ is hydrogen, -OR_E, =O, -C(=O)R_E, -CO₂R_E, -CN, -SCN, halogen, -SR_E, -SOR_E, -SO₂R_E, -NO₂, -N(R_E)₂, -NHC(O)R_E, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R₃ is hydrogen, a nitrogen protecting group, -COOR_F, -COR_F, -CN, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

1 wherein R₄ and R₆ are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
2 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

3 wherein R₅ and R₇ are each independently hydrogen, -OR_G, -C(=O)R_G, -CO₂R_G, -CN, -
4 SCN, halogen, -SR_G, -SOR_G, -SO₂R_G, -NO₂, -N(R_G)₂, -NHC(O)R_G, or an aliphatic,
5 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently
6 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
7 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

8 wherein R₈ is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH,
9 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

10 wherein m is 0-5;

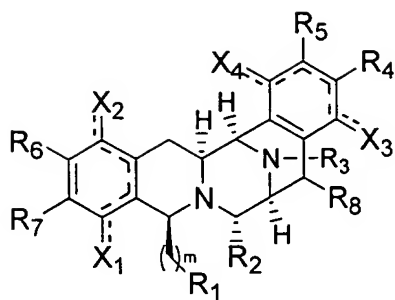
11 wherein X₁, X₂, X₃ and X₄ are each independently hydrogen, -OR_H, =O, -C(=O)R_H,
12 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an
13 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
14 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
15 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

16 whereby if at least either X₁ and X₂ or X₃ and X₄ are doubly bonded to the 6-membered
17 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
18 and one double bond, and a quinone moiety is generated, or if at least either X₁ and X₂ or X₃ and
19 X₄ are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
20 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
21 generated;

22 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
23 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
24 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
25 unsubstituted; and

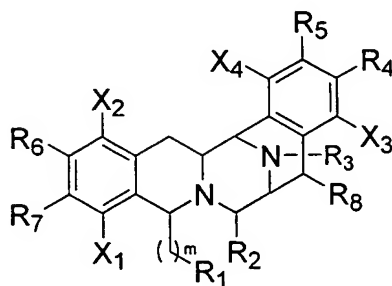
26 pharmaceutically acceptable derivatives thereof.

27
28 2. The compound of claim 1, wherein the compound has the stereochemistry and structure
29 of formula (Ia):



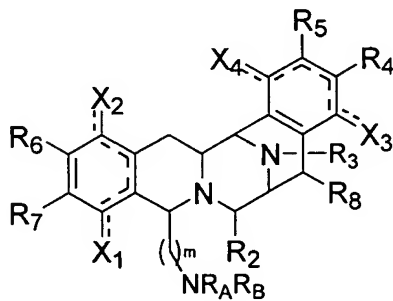
(Ia)

3. The compound of claim 1, wherein the compound has the structure (II):



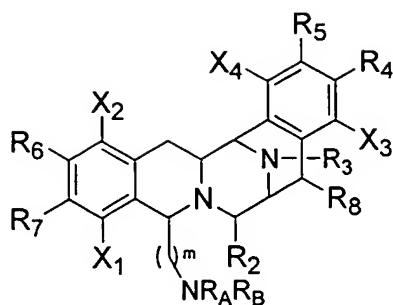
(II)

4. The compound of claim 1, wherein the compound has the structure (III):



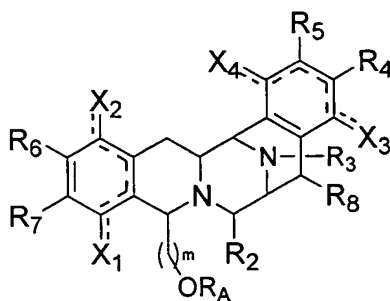
(III)

5. The compound of claim 1, wherein the compound has the structure (IV):



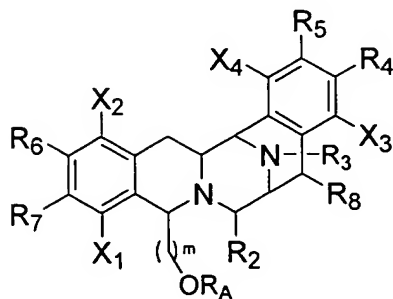
(IV)

6. The compound of claim 1, wherein the compound has the structure (V):



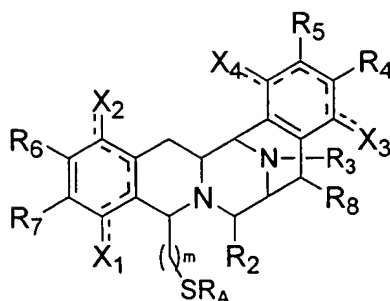
(V)

7. The compound of claim 1, wherein the compound has the structure (VI):



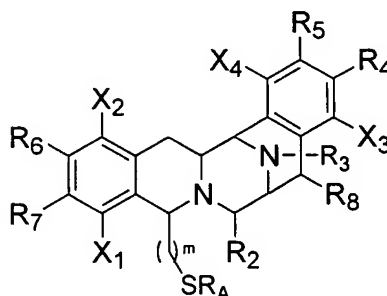
(VI)

8. The compound of claim 1, wherein the compound has the general structure (VII):



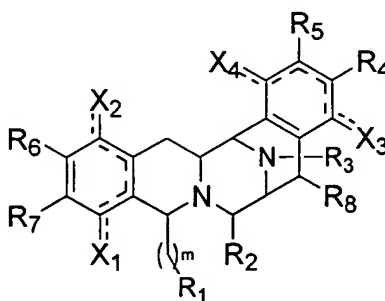
(VII)

9. The compound of claim 1, wherein the compound has the general structure (VIII):



(VIII)

10. The compound of claim 1, wherein the compound has the general structure (IX):

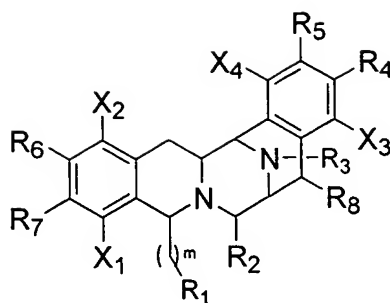


(IX)

wherein R_1 is a substituted or unsubstituted, cyclic or acyclic, branched or unbranched aliphatic or heteroaliphatic moiety, or is a substituted or unsubstituted aryl or heteroaryl moiety.

11. The compound of claim 1, wherein the compound has the general structure (X):

1



(X)

2

3

4

5 wherein R_1 is a substituted or unsubstituted, cyclic or acyclic, branched or unbranched
6 aliphatic or heteroaliphatic moiety, or is a substituted or unsubstituted aryl or heteroaryl moiety.

7

8 12. The compound of claim 1, having one or more of the following limitations:

9 when m is 1, R_1 excludes any one or more of the following groups: -NH(protecting
10 group), $-NH_2$, $-NHCOCOMe$, $-NHCOC(Me)(OMe)(OMe)$, $-NHCOCH(NH_2)CH_3$, -
11 $NHCOCH(NH(acyl))CH_3$, $-NHCOCH(NH_2)Ac$, or $NHCOCH(NHCOOBn)(Me)$; -
12 $O(C=O)C(CH_3)=C(CH_3)H$; $-OH$, $-O(protecting\ group)$, $-O(COCH_3)$, $-O(C=O)CH_2CH_3$; or

13 when m is 1; when X_1 , X_2 , X_3 and X_4 are each $=O$; when R_2 is $-CN$ or $-OH$; when R_4 and
14 R_6 are each $-CH_3$; when R_5 and R_7 are each $-OCH_3$; when R_8 is H ; and R_1 is $-NH(C=O)R_C$, then
15 R_C is not $-CH(NR_W R_Y)(CH_2 R_Z)$ where R_W and R_Y are each independently hydrogen or C_{1-7}
16 alkyl, aryl(C_{1-4})alkyl, (C_{1-4})alkylaryl, a substituted sulfonyl ($-S(O)_2-$) group, or a substituted acyl
17 group, and where R_Z is hydrogen or C_{1-4} alkyl; or

18 when m is 1; when X_1 , X_2 , X_3 and X_4 are each $=O$; when R_2 is $-CN$; when R_4 and R_6 are
19 each $-CH_3$; when R_5 and R_7 are each $-OCH_3$; when R_8 is H ; and R_1 is $-NH(C=O)R_C$, then R_C is
20 not $-C(OH)(Me)CH_2(C=O)Me$; or

21 when m is 1 and when R_2 is H ; and R_1 is $-NH(C=O)R_C$, then R_C is not -
22 $CH(Me)NH(C=O)O(CH_2)Ph$; or

23 when m is 0; R_2 is H ; X_3 is H ; and R_1 is $-C(=O)R_A$, then R_A is not $-O(alkyl)$; or

24 when R_2 is H ; m is 1; and R_1 is $-OR_A$, then R_A is not $-C(=O)R_C$, or $S(O)_2 R_C$, wherein R_C
25 is an alkyl moiety.

26

1 13. The compound of claim 1, wherein m is 0 or 1.

2
3 14. The compound of claim 1, wherein R₂ is CN, -SCN, =O, OH, protected hydroxyl, H, or
4 alkoxy.

5
6 15. The compound of claim 1, wherein R₂ is hydrogen, hydroxyl, -CN or -SCN.

7
8 16. The compound of claim 1, wherein R₈ is hydrogen.

9
10 17. The compound of claim 1, wherein X₁, X₂, X₃, and X₄ are each independently alkoxy,
11 OH, protected hydroxyl, or =O.

12
13 18. The compound of claim 1, wherein R₂ is CN, -SCN, =O, OH, protected hydroxyl, H, or
14 alkoxy; R₃ is hydrogen, a nitrogen protecting group, -CN, aliphatic, or aryl; R₄ and R₆ are each
15 alkyl; R₅ and R₇ are each alkyloxy or thioalkyl; R₈ is hydrogen, alkyl, -OH, protected hydroxyl,
16 =O, CN, halogen, SH, alkoxy, thioalkyl, amino, or alkylamino; and X₁, X₂, X₃, and X₄ are each
17 independently alkoxy, OH or =O.

18
19 19. The compound of claim 1, wherein R₂ is -CN, -SCN, -OH, protected hydroxyl, H, or
20 alkoxy; R₃ is hydrogen, a nitrogen protecting group, aliphatic, or aryl; R₄ and R₆ are each alkyl;
21 R₅ and R₇ are each alkyloxy or thioalkyl; X₁ and X₄ are each -OH; R₈ is hydrogen, alkyl, OH,
22 protected hydroxyl, =O, CN, halogen, SH, alkoxy, thioalkyl, amino, or alkylamino; and X₂ and
23 X₃ are each alkyloxy or thioalkyl.

24
25 20. The compound of claim 1, wherein X₁ is OH, X₂ is OCH₃, X₃ is OCH₃, X₄ is OH, R₂ is
26 CN, H or OH, R₃ is Me, R₄ is CH₃, R₅ is OCH₃, R₆ is CH₃, R₇ is OCH₃, and R₈ is H.

27
28 21. The compound of claim 1, wherein R₁ is OR_A, SR_A, or NR_AR_B, wherein R_A and R_B are
29 each independently hydrogen, -(C=O)R_C or an aliphatic, heteroaliphatic, aryl, or heteroaryl
30 moiety, wherein R_C is -(C=O)R_D, or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety, and

1 wherein R_D is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or wherein R_A and R_B ,
2 taken together, form a heterocyclic moiety,

3 whereby each of said aliphatic and heteroaliphatic moieties is independently
4 substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of said aryl,
5 heteroaryl and heterocyclic moieties is independently substituted or unsubstituted.

6
7 22. The compound of claim 1, wherein R_1 is OR_A , SR_A , or NR_AR_B , wherein R_A and R_B are
8 each independently hydrogen, $-(C=O)R_C$, or an aryl, (aliphatic)aryl, (heteroaliphatic)aryl,
9 heteroaryl, (aliphatic)heteroaryl, or (heteroaliphatic)heteroaryl moiety, wherein R_C is an aryl,
10 (aliphatic)aryl, (heteroaliphatic)aryl, heteroaryl, (aliphatic)heteroaryl, or
11 (heteroaliphatic)heteroaryl moiety, or wherein R_A and R_B taken together form a heterocyclic
12 moiety,

13 whereby each of said aliphatic and heteroaliphatic moieties is independently substituted
14 or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of said aryl, heteroaryl
15 and heterocyclic moieties is independently substituted or unsubstituted.

16
17 23. The compound of claim 1, wherein R_1 is $-NR_AC(=O)R_C$, wherein R_A is hydrogen or
18 lower alkyl, and R_C is a substituted or unsubstituted, branched or unbranched, cyclic or acyclic
19 aliphatic or heteroaliphatic moiety, or a substituted or unsubstituted aryl or heteroaryl moiety, or
20 wherein R_A and R_C taken together form a heterocyclic or heteroaryl moiety.

21
22 24. The compound of claim 1, wherein R_1 is $NR_AC(=O)R_C$, wherein R_A is hydrogen or lower
23 alkyl, and R_C is an aryl, (aliphatic)aryl, (aliphatic)heteroaryl, heteroaryl, (heteroaliphatic)aryl, or
24 (heteroaliphatic)heteroaryl moiety, or wherein R_A and R_C taken together form a heterocyclic or
25 heteroaryl moiety;

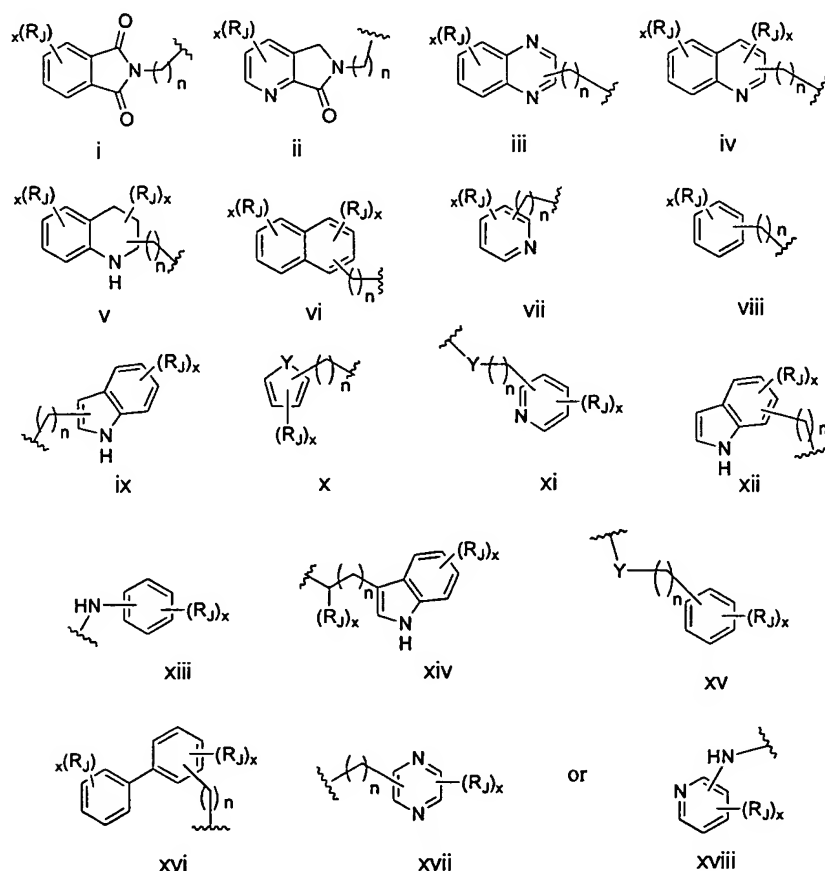
26 whereby each of said aliphatic and heteroaliphatic moieties is independently
27 substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of
28 said aryl, heteroaryl and heterocyclic moieties is independently substituted or
29 unsubstituted.

25. The compound of claim 1, wherein R_1 is a substituted or unsubstituted, branched or unbranched, cyclic or acyclic aliphatic or heteroaliphatic moiety, or a substituted or unsubstituted aryl or heteroaryl moiety.

26. The compound of claim 1, wherein R_1 is an aryl, (aliphatic)aryl, (aliphatic)heteroaryl, heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety;

whereby each of said aliphatic and heteroaliphatic moieties is independently substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of said aryl, heteroaryl and heterocyclic moieties is independently substituted or unsubstituted;

27. The compound of claim 1, wherein any one or more of R_1 , R_A , R_B , R_C , or R_D is independently any one of the following groups:

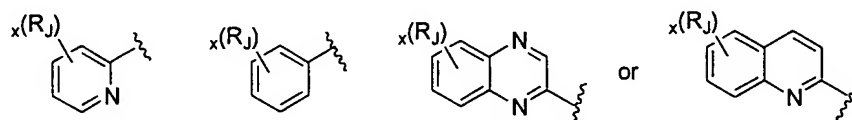


wherein each occurrence of R_J is independently hydrogen, a protecting group, $-OR_K$, $=O$, $-C(=O)R_K$, $-CO_2R_K$, $-CN$, $-SCN$, halogen, $-SR_K$, $-SOR_K$, $-SO_2R_K$, $-NO_2$, $-N(R_K)_2$, $-NHC(O)R_K$, $-B(OR_K)_2$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_K is independently hydrogen, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or wherein two occurrences of R_K , taken together form a cyclic aliphatic or heteroaliphatic moiety; wherein each occurrence of Y is independently O , S or NH ; wherein each occurrence of x is independently 0-5; and wherein each occurrence of n is independently 0-3, or wherein R_J is a labeling reagent,

whereby each of said aliphatic and heteroaliphatic moieties are independently substituted or unsubstituted, branched or unbranched or cyclic or acyclic, and each of said aryl and heteroaryl moieties is independently substituted or unsubstituted.

28. The compound of claim 27, wherein R_I is NR_AR_B , R_A is hydrogen, R_B is $-(C=O)R_C$, and R_C is iii, iv, vii, viii, ix, x, xv, or xvii, or R_A and R_C taken together form the structure of i or ii.

29. The compound of claim 27, wherein R_I is NR_AR_B and R_A is hydrogen, R_B is $-(C=O)R_C$, and R_C is



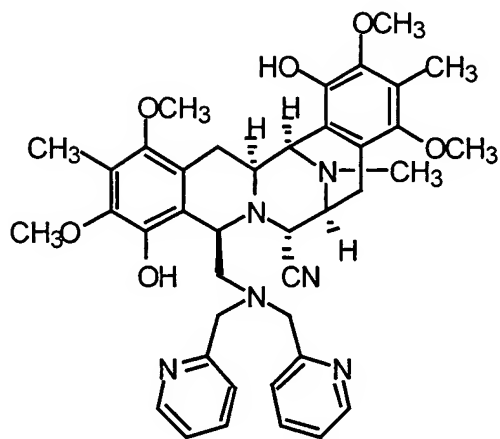
30. The compound of claim 27, 28 or 29, wherein R_J is hydrogen, halogen, $-OH$, lower alkyl or lower alkoxy.

31. The compound of claim 27, 28 or 29, wherein R_J is a linker-biotin or a linker-fluorescein moiety.

32. The compound of claim 27, 28 or 29, wherein x is 1 or 2.

1 33. The compound of claim 1, wherein the compound has the structure:

2

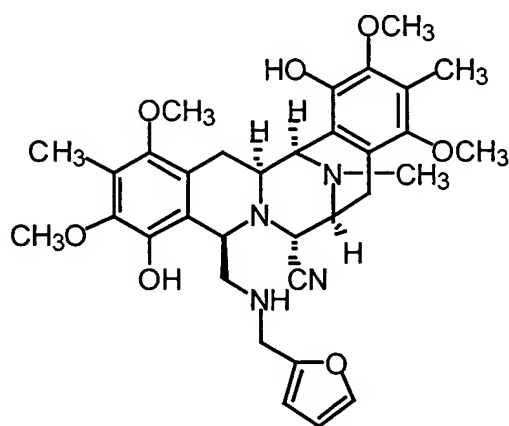


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5 34. The compound of claim 1, wherein said compound has the structure:

6

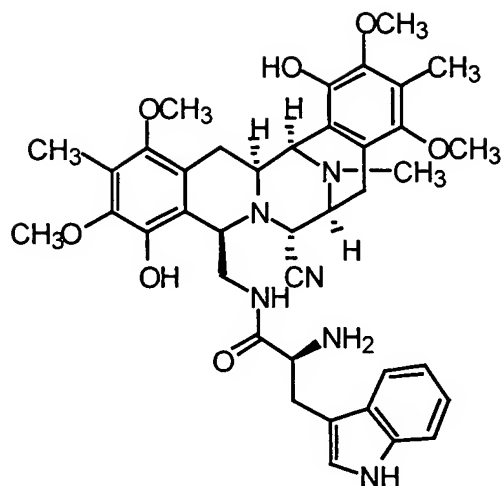


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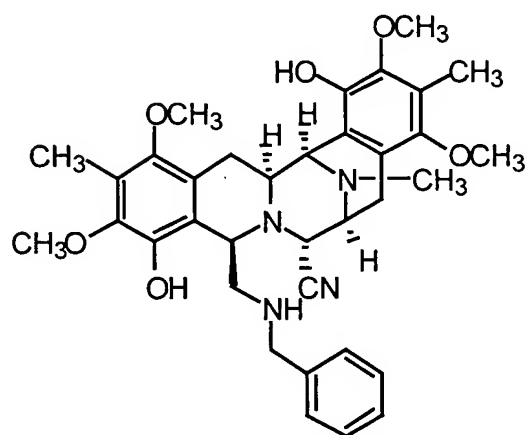
9 35. The compound of claim 1, wherein the compound has the structure:

10



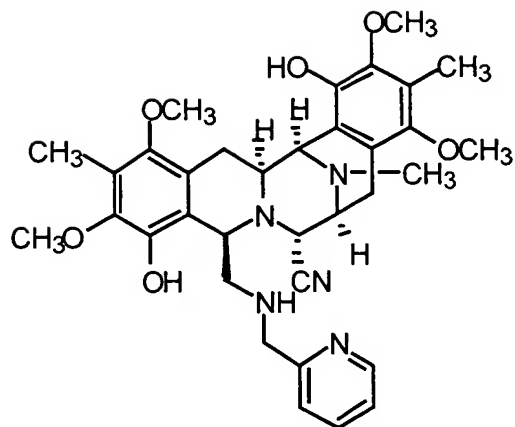
1
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36. The compound of claim 1, wherein the compound has the structure:

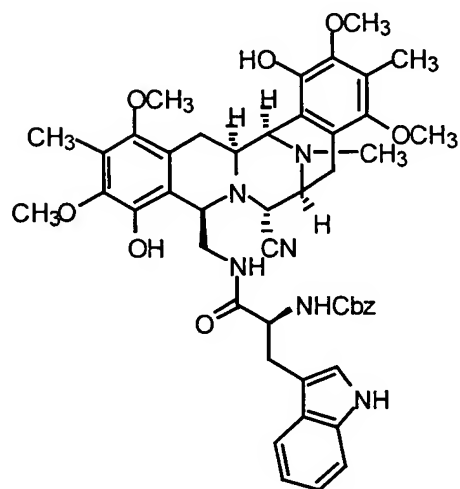


5
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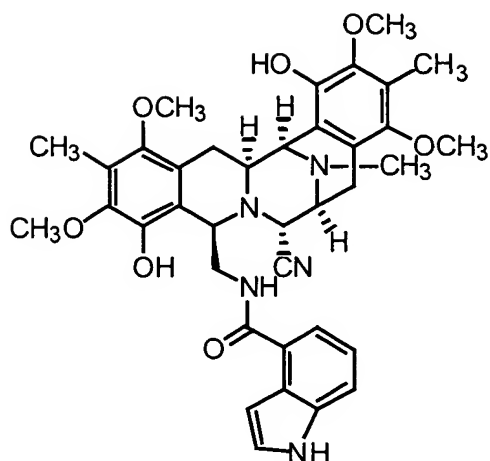
37. The compound of claim 1, wherein the compound has the structure:



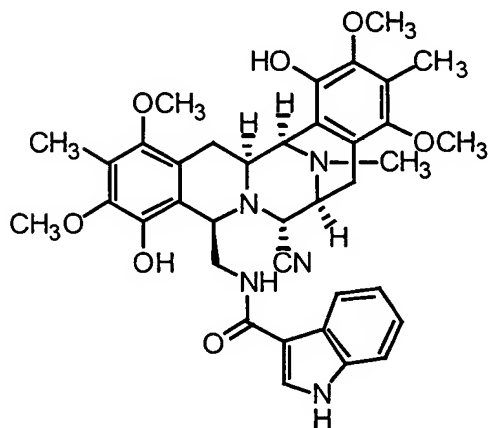
38. The compound of claim 1, wherein said compound has the structure:



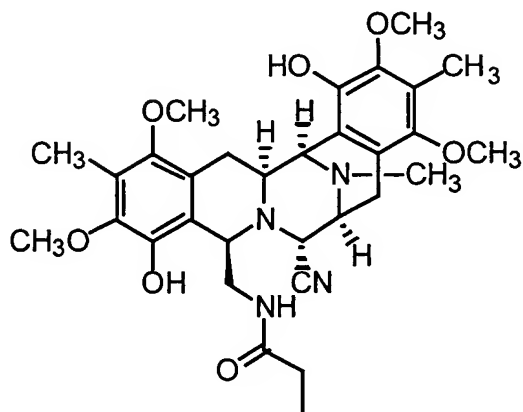
39. The compound of claim 1, wherein the compound has the structure:



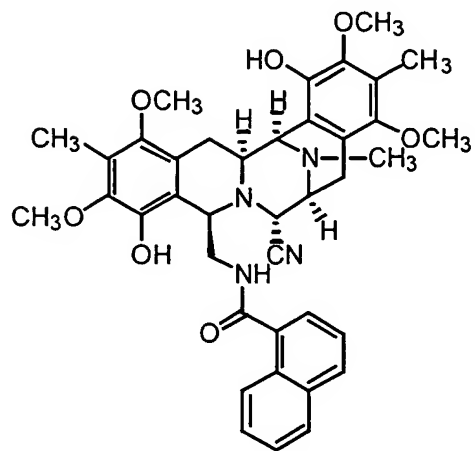
40. The compound of claim 1, wherein the compound has the structure:



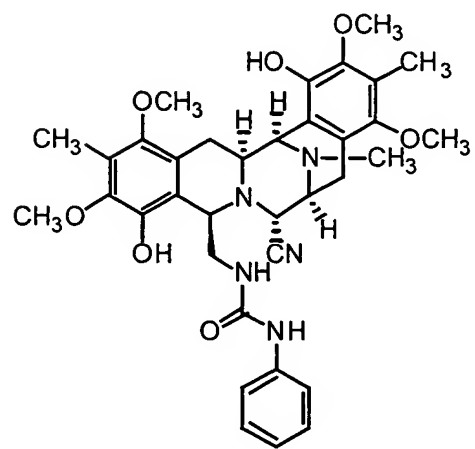
41. The compound of claim 1, wherein the compound has the structure:



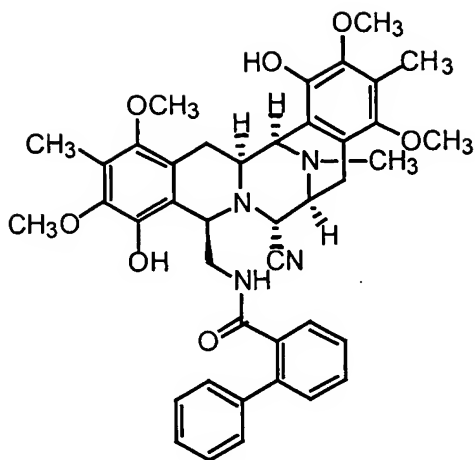
42. The compound of claim 1, wherein the compound has the structure:



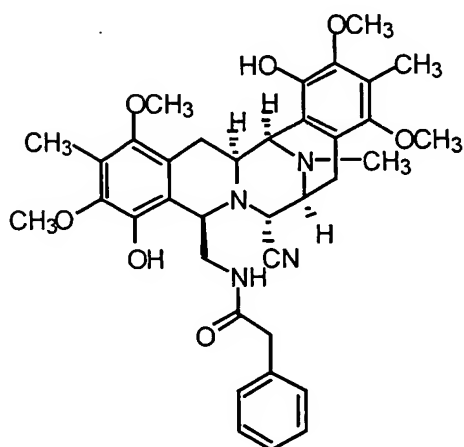
43. The compound of claim 1, wherein the compound has the structure:



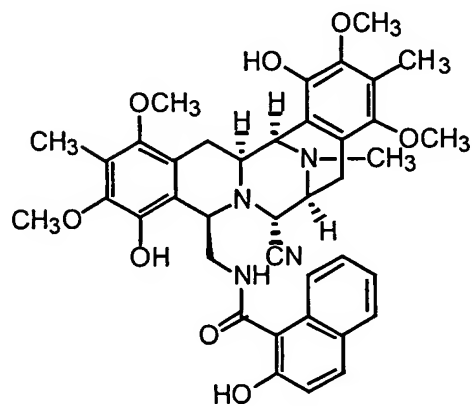
44. The compound of claim 1, wherein the compound has the structure:



45. The compound of claim 1, wherein the compound has the structure:

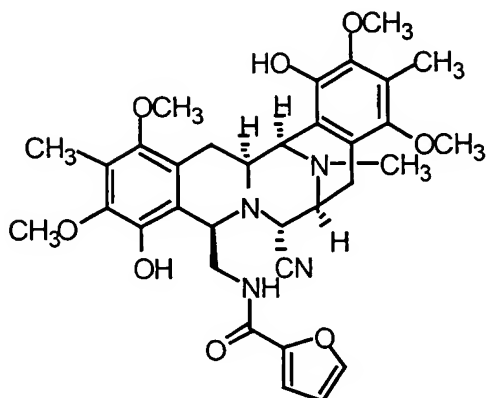


46. The compound of claim 1, wherein the compound has the structure:



1 47. The compound of claim 1, wherein the compound has the structure:

2

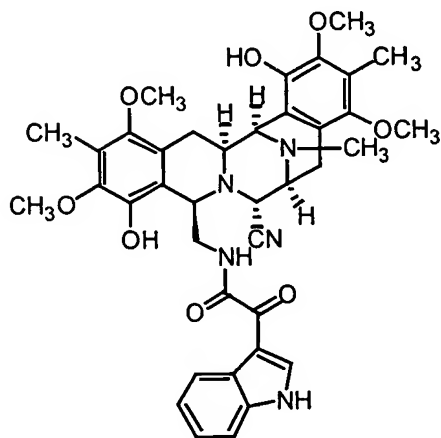


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5 48. The compound of claim 1, wherein the compound has the structure:

6

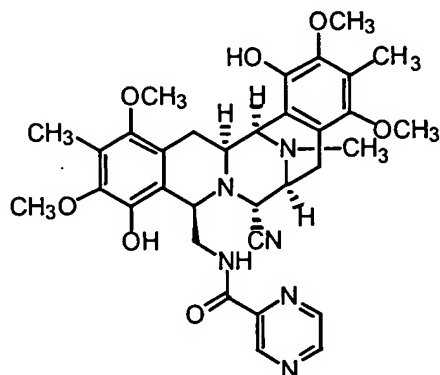


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9 49. The compound of claim 1, wherein the compound has the structure:

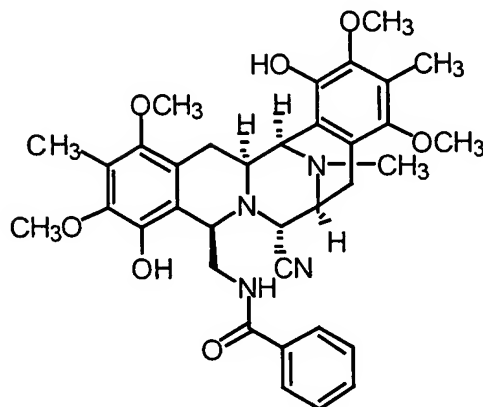
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1 50. The compound of claim 1, wherein the compound has the structure:

2



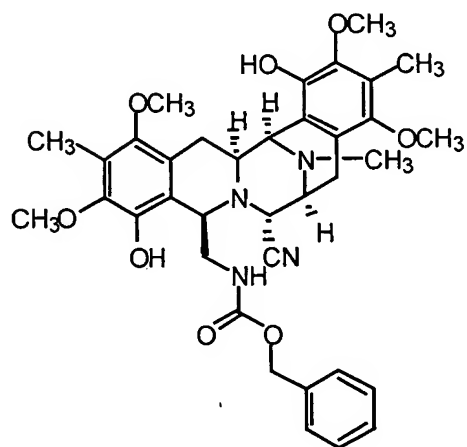
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6 51. The compound of claim 1, wherein the compound has the structure:

7

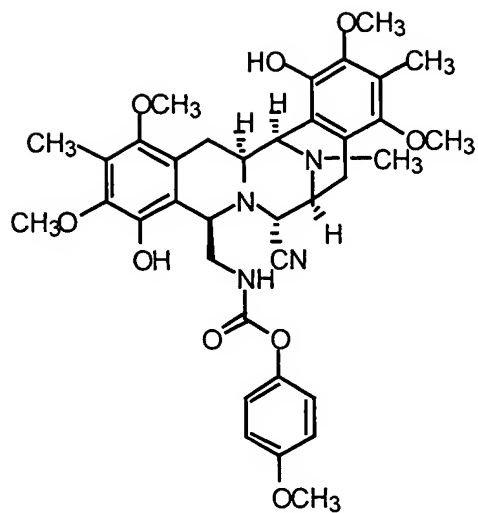


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10 52. The compound of claim 1, wherein the compound has the structure:

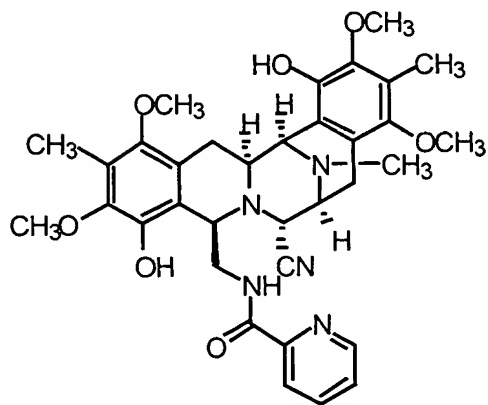
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3 53. The compound of claim 1, wherein the compound has the structure:

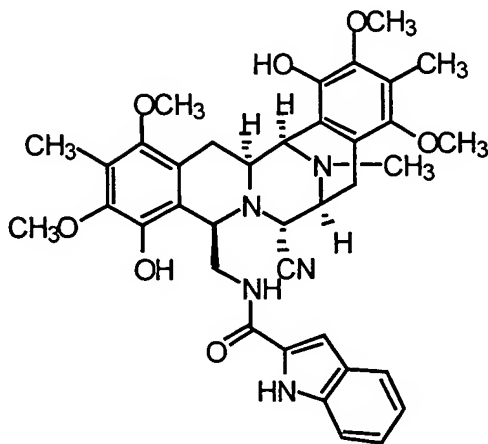


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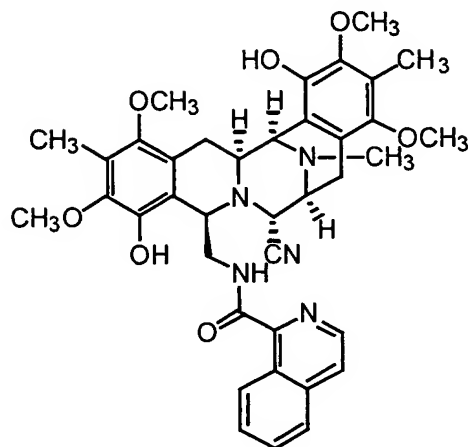
6 54. The compound of claim 1, wherein the compound has the structure:

7

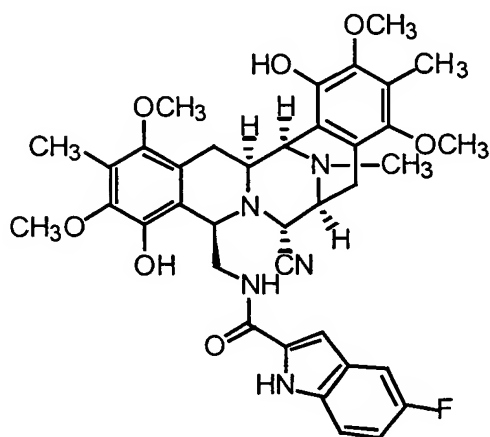


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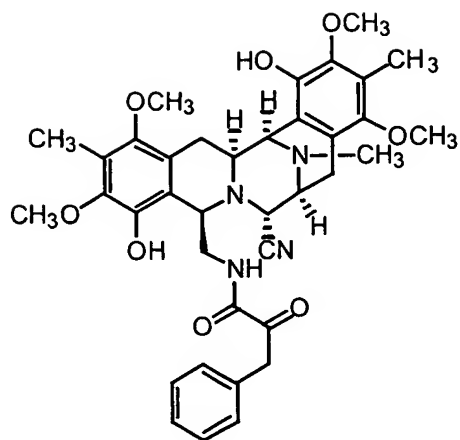
- 1 55. The compound of claim 1, wherein the compound has the structure:
2



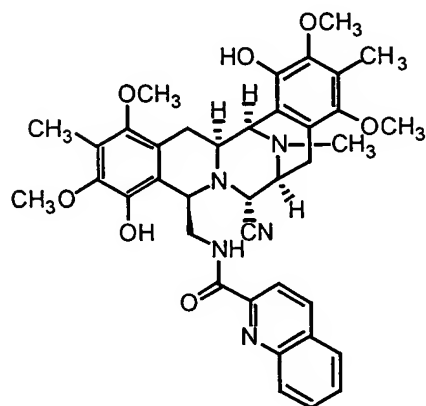
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4
5 56. The compound of claim 1, wherein the compound has the structure:
6



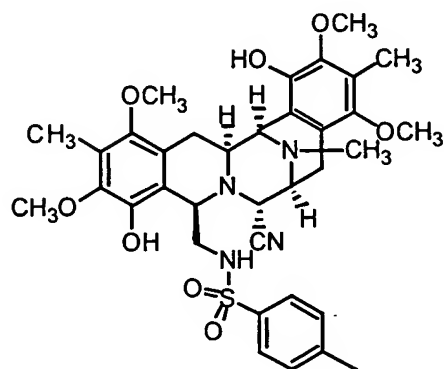
- 7
8
9 57. The compound of claim 1, wherein the compound has the structure:
10



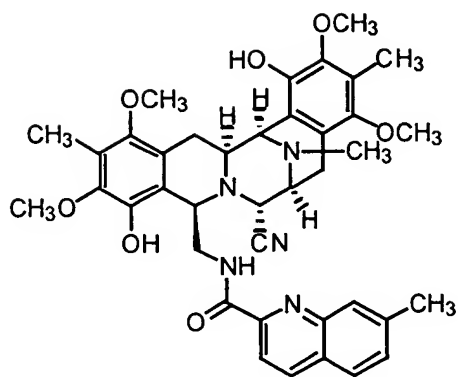
58. The compound of claim 1, wherein the compound has the structure:



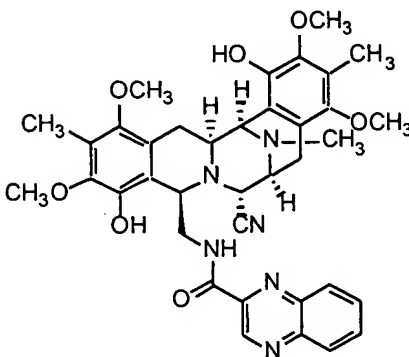
59. The compound of claim 1, wherein the compound has the structure:



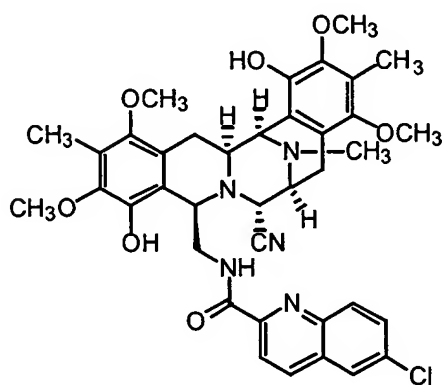
60. The compound of claim 1, wherein the compound has the structure:



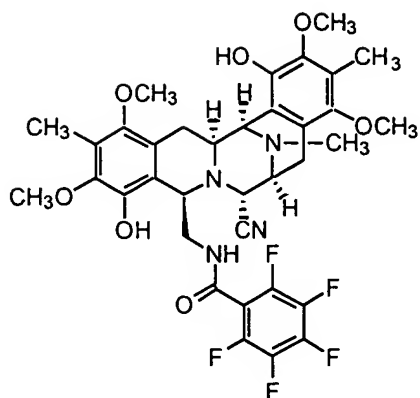
61. The compound of claim 1, wherein the compound has the structure:



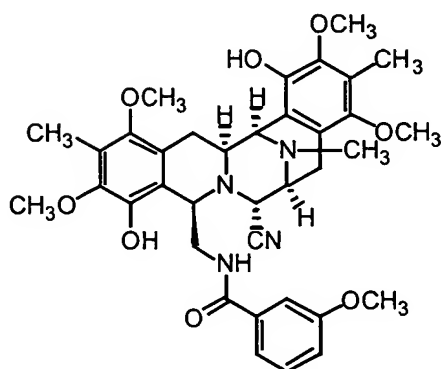
62. The compound of claim 1, wherein the compound has the structure:



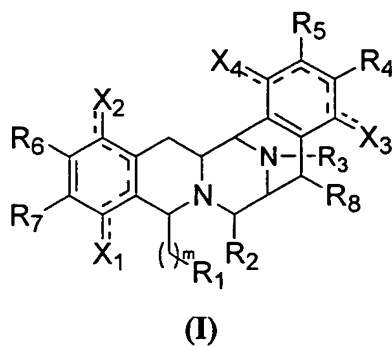
63. The compound of claim 1, wherein the compound has the structure:



64. The compound of claim 1, wherein the compound has the structure:



65. A pharmaceutical composition comprising:
a compound having the structure (I):



1 wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic,
2 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
3 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
4 hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
5 moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or
6 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-$
7 SR_D , $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
8 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
9 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
10 moiety;

11 wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-$
12 SOR_E , $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
13 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
14 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
15 heteroaryloxy, or heteroarylthio moiety;

16 wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an
17 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
18 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
19 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

20 wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
21 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

22 wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-$
23 SCN , halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic,
24 heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently
25 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
26 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

27 wherein R_8 is hydrogen, alkyl, $-OH$, protected hydroxyl, $=O$, $-CN$, $-SCN$, halogen, $-SH$,
28 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

29 wherein m is 0-5;

30 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, $-OR_H$, $=O$, $-C(=O)R_H$,

1 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an
2 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
3 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
4 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

5 whereby if at least either X₁ and X₂ or X₃ and X₄ are doubly bonded to the 6-membered
6 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
7 and one double bond, and a quinone moiety is generated, or if at least either X₁ and X₂ or X₃ and
8 X₄ are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
9 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
10 generated;

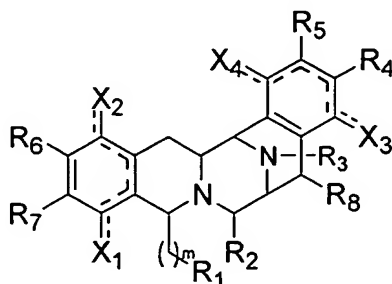
11 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
12 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
13 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
14 unsubstituted, and pharmaceutically acceptable derivatives thereof; and

15 a pharmaceutically acceptable carrier or diluent.

16
17 66. The pharmaceutical composition of claim 65, wherein the pharmaceutical composition
18 optionally further comprises one or more additional therapeutic agents.

19
20 67. The pharmaceutical composition of claim 66, wherein said composition further comprises
21 one or more cytotoxic agents.

22
23 68. A method for inhibiting the growth of or killing cancer cells comprising:
24 contacting the cells with an amount of a composition effective to inhibit the growth of or
25 to kill cancer cells, the composition comprising a compound of formula (I) or pharmaceutically
26 derivatives thereof:



(I)

wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-SR_D$, $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-SOR_E$, $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-SCN$, halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_8 is hydrogen, alkyl, $-OH$, protected hydroxyl, $=O$, $-CN$, $-SCN$, halogen, $-SH$, protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

wherein m is 0-5;

1 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, $-OR_H$, $=O$, $-C(=O)R_H$,
2 $-CO_2R_H$, $-CN$, $-SCN$, halogen, $-SR_H$, $-SOR_H$, $-SO_2R_H$, $-NO_2$, $-N(R_H)_2$, $-NHC(O)R_H$, or an
3 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
4 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
5 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

6 whereby if at least either X_1 and X_2 or X_3 and X_4 are doubly bonded to the 6-membered
7 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
8 and one double bond, and a quinone moiety is generated, or if at least either X_1 and X_2 or X_3 and
9 X_4 are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
10 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
11 generated;

12 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
13 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
14 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
15 unsubstituted; and pharmaceutically acceptable derivatives thereof; and

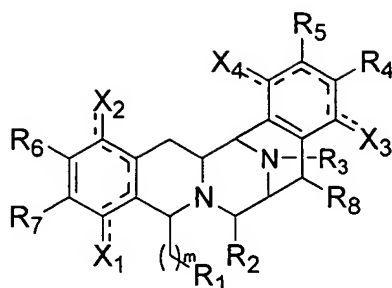
16 optionally further comprising a pharmaceutically acceptable carrier or diluent.

17
18 69. The method of claim 68, wherein said composition further comprises one or more
19 additional therapeutic agents.

20
21 70. The method of claim 69, wherein said composition further comprises one or more
22 cytotoxic agents.

23
24 71. The method of claim 68, wherein the cancer cells comprise melanoma cancer cells or
25 lung cancer cells.

26
27 72. A method for treating cancer comprising:
28 administering to a subject in need thereof a therapeutically effective amount of a
29 composition comprising a compound of formula (I) or pharmaceutically acceptable derivatives
30 thereof;



(I)

wherein R_1 is NR_AR_B , $-OR_A$, $-SR_A$, $-C(=O)R_A$, $-C(=S)R_A$, $-S(O)_2R_A$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently hydrogen, $-(C=O)R_C$, $-NHR_C$, $-(SO_2)R_C$, $-OR_C$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or R_A and R_B , when taken together form an aryl, heteroaryl, cycloaliphatic, or cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, $-OR_D$, $-SR_D$, $-NHR_D$, $-(C=O)R_D$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_2 is hydrogen, $-OR_E$, $=O$, $-C(=O)R_E$, $-CO_2R_E$, $-CN$, $-SCN$, halogen, $-SR_E$, $-SOR_E$, $-SO_2R_E$, $-NO_2$, $-N(R_E)_2$, $-NHC(O)R_E$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_3 is hydrogen, a nitrogen protecting group, $-COOR_F$, $-COR_F$, $-CN$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_4 and R_6 are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_5 and R_7 are each independently hydrogen, $-OR_G$, $-C(=O)R_G$, $-CO_2R_G$, $-CN$, $-SCN$, halogen, $-SR_G$, $-SOR_G$, $-SO_2R_G$, $-NO_2$, $-N(R_G)_2$, $-NHC(O)R_G$, or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently

1 hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy,
2 aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

3 wherein R_8 is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH,
4 protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

5 wherein m is 0-5;

6 wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, -OR_H, =O, -C(=O)R_H,
7 -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an
8 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is
9 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
10 acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

11 whereby if at least either X_1 and X_2 or X_3 and X_4 are doubly bonded to the 6-membered
12 ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds
13 and one double bond, and a quinone moiety is generated, or if at least either X_1 and X_2 or X_3 and
14 X_4 are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-
15 membered rings represent two double bonds and one single bond, and a hydroquinone moiety is
16 generated;

17 whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may
18 independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and
19 each of the foregoing aryl or heteroaryl moieties may independently be substituted or
20 unsubstituted; and

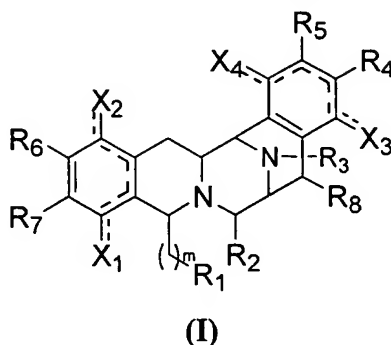
21 optionally further comprising a pharmaceutically acceptable carrier or diluent.

22
23 73. The method of claim 72, wherein said composition further comprises one or more
24 additional therapeutic agents.

25
26 74. The method of claim 73, wherein said composition further comprises one or more
27 cytotoxic agents.

28
29 75. The method of claim 72, wherein the cancer cells comprise melanoma cancer cells or
30 lung cancer cells.

1 76. A method for the synthesis of a compound having the formula (I):



2
3
4
5 wherein R₁ is NR_AR_B, -OR_A, -SR_A, -C(=O)R_A, -C(=S)R_A, -S(O)₂R_A, or an aliphatic,
6 heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or
7 (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_A and R_B is independently
8 hydrogen, -(C=O)R_C, -NHR_C, -(SO₂)R_C, -OR_C, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
9 moiety, or R_A and R_B, when taken together form an aryl, heteroaryl, cycloaliphatic, or
10 cycloheteroaliphatic moiety, wherein each occurrence of R_C is independently hydrogen, -OR_D, -
11 SR_D, -NHR_D, -(C=O)R_D, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each
12 occurrence of R_D is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic,
13 aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio
14 moiety;

15 wherein R₂ is hydrogen, -OR_E, =O, -C(=O)R_E, -CO₂R_E, -CN, -SCN, halogen, -SR_E, -
16 SOR_E, -SO₂R_E, -NO₂, -N(R_E)₂, -NHC(O)R_E, or an aliphatic, heteroaliphatic, aryl, or heteroaryl
17 moiety, wherein each occurrence of R_E is independently hydrogen, a protecting group, or an
18 aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio,
19 heteroaryloxy, or heteroarylthio moiety;

20 wherein R₃ is hydrogen, a nitrogen protecting group, -COOR_F, -COR_F, -CN, or an
21 aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_F is
22 independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl,
23 alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

24 wherein R₄ and R₆ are each independently hydrogen, or an aliphatic, heteroaliphatic, aryl,
25 heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

26 wherein R₅ and R₇ are each independently hydrogen, -OR_G, -C(=O)R_G, -CO₂R_G, -CN, -
27 SCN, halogen, -SR_G, -SOR_G, -SO₂R_G, -NO₂, -N(R_G)₂, -NHC(O)R_G, or an aliphatic,

heteroaliphatic, aryl or heteroaryl moiety, wherein each occurrence of R_G is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

wherein R_8 is hydrogen, alkyl, -OH, protected hydroxyl, =O, -CN, -SCN, halogen, -SH, protected thio, alkoxy, thioalkyl, amino, protected amino, or alkylamino;

wherein m is 0-5;

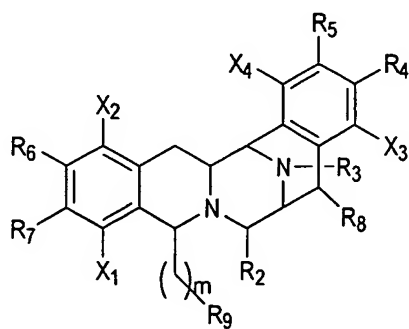
wherein X_1 , X_2 , X_3 and X_4 are each independently hydrogen, -OR_H, =O, -C(=O)R_H, -CO₂R_H, -CN, -SCN, halogen, -SR_H, -SOR_H, -SO₂R_H, -NO₂, -N(R_H)₂, -NHC(O)R_H, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_H is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety;

or wherein X_1 and R_7 taken together comprise a heterocyclic moiety;

whereby if at least either X_1 and X_2 or X_3 and X_4 are doubly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-membered rings represent two single bonds and one double bond, and a quinone moiety is generated, or if at least either X_1 and X_2 or X_3 and X_4 are singly bonded to the 6-membered ring, then the dotted bonds in either or both of the 6-membered rings represent two double bonds and one single bond, and a hydroquinone moiety is generated;

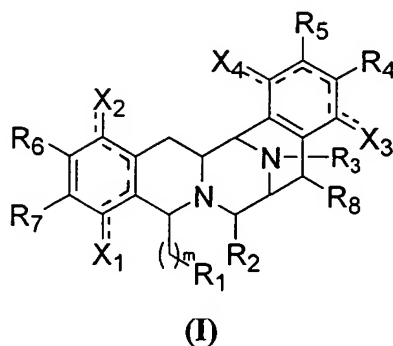
whereby each of the foregoing aliphatic, heteroaliphatic and alkyl moieties may independently be substituted or unsubstituted, branched or unbranched, or cyclic or acyclic, and each of the foregoing aryl or heteroaryl moieties may independently be substituted or unsubstituted; wherein said method comprises:

(a) providing a compound of formula (XV)



(XV); and

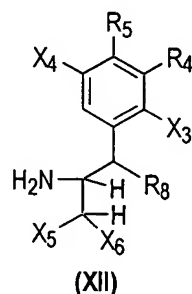
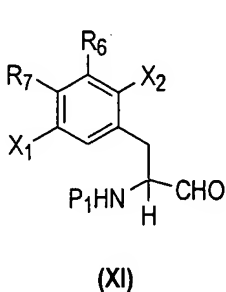
(b) reacting said compound of formula (XV) under suitable conditions to generate a compound of formula (I):



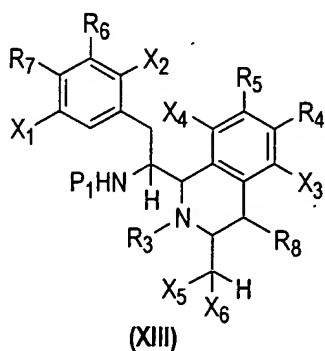
wherein X₁-X₄, R₁-R₈, and m are as described above and in classes and subclasses herein,
and

wherein the step of providing a compound of formula (XV) further comprises:

(1) reacting a first N-protected and a second C-protected α -amino aldehyde precursor having the structures:

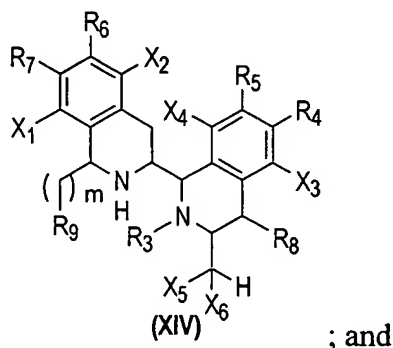


under suitable conditions to generate a tetrahydroisoquinoline core having the structure (IX):



(2) optionally reacting said tetrahydroisoquinoline core under suitable conditions to diversify R₃;

(3) reacting a third aldehyde precursor having the structure: $R_9(CH_2)_mCHO$, with said tetrahydroisoquinoline core structure (XIV) under suitable conditions to generate a trimer of aldehydes having the structure:



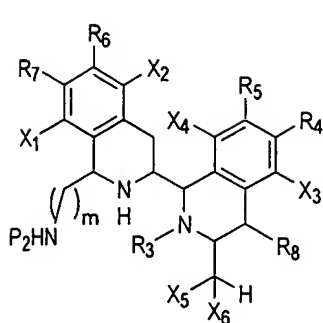
(4) reacting said trimer of aldehydes under suitable conditions to generate a compound of structure (XV),

wherein P_1 is hydrogen or a nitrogen protecting group;

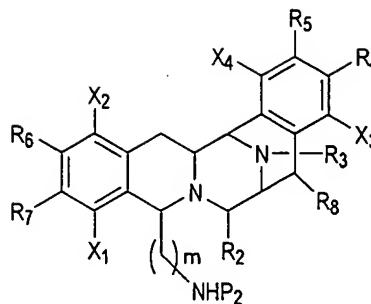
X_5 and X_6 taken together represent a carbon protecting group, optionally substituted with a solid support unit; and

R_9 is NR_LR_M , $-OR_L$, $-SR_L$, $-C(=O)R_L$, $-C(=S)R_L$, $-S(O)_2R_L$, or an aliphatic, heteroaliphatic, aryl, heteroaryl, (aliphatic)aryl, (aliphatic)heteroaryl, (heteroaliphatic)aryl, or (heteroaliphatic)heteroaryl moiety, wherein each occurrence of R_L and R_M is independently hydrogen, $-(C=O)R_N$, $-NHR_N$, $-(SO_2)R_N$, $-OR_N$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, or R_L and R_M , when taken together form an aryl, heteroaryl, cycloaliphatic, or cycloheteroaliphatic moiety, wherein each occurrence of R_N is independently hydrogen, $-OR_P$, $-SR_P$, $-NHR_P$, $-(C=O)R_P$, or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety, wherein each occurrence of R_P is independently hydrogen, a protecting group, or an aliphatic, heteroaliphatic, aryl, heteroaryl, acyl, alkoxy, aryloxy, alkylthio, arylthio, heteroaryloxy, or heteroarylthio moiety.

77. The method of claim 76, wherein for the intermediates (XIV) and (XV) R_9 is $-NHP_2$, P_2 is a nitrogen protecting group, and the intermediates have the structures (XIVa) and (XVa):



(XIVa)



(XVa)

78. The method of claim 76, wherein $R_9(CH_2)_mCHO$ is (aliphatic)(C=O)(CH₂)_mCHO, (heteroaliphatic)(C=O)(CH₂)_mCHO, (aliphatic)(CH₂)_mCHO, (heteroaliphatic)(CH₂)_mCHO, aryl(aliphatic)(CH₂)_mCHO, aryl(heteroaliphatic)(CH₂)_mCHO, -heteroaryl(aliphatic)(CH₂)_mCHO, or heteroaryl(heteroaliphatic)(CH₂)_mCHO,

wherein each of the aliphatic, and heteroaliphatic moieties is independently cyclic or acyclic, linear or branched, or substituted or unsubstituted and wherein the aryl and heteroaryl moieties are independently substituted or unsubstituted.

79. The method of claim 76, wherein $R_9(CH_2)_mCHO$ is CH₃(CH₂)₁₋₆CHO; (protecting group)O(CH₂)₁₋₆CHO; (protecting group)NH(CH₂)₁₋₆CHO; (protecting group)S(CH₂)₁₋₆CHO; (alkyl)O(C=O)CHO; (aryl)(alkenyl)CHO; (heteroaryl)(alkenyl)CHO; (aryl)CHO; or (heteroaryl)CHO,

wherein each of the aliphatic, and heteroaliphatic moieties is independently cyclic or acyclic, linear or branched, or substituted or unsubstituted and wherein the aryl and heteroaryl moieties are independently substituted or unsubstituted.

80. The method of claim 76, wherein X₅ is CN and X₆ is a heterocyclic moiety optionally substituted with a solid support unit.

81. The method of claim 76, wherein the alkaloid structure (I) generated is that of saframycin A.

1 82. The method of claim 76, wherein the method is stereoselective and the alkaloid structure
2 **(I)** generated is that of -(-) saframycin A.

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